REMARKS

A Petition to Extend Time under 37 C.F.R. § 1.136(a) for one (1) month, up to and including Tuesday, September 7, 2004, is enclosed.

Claims 50-68 and 70-77 are currently amended. No new matter is added through these amendments. More specifically, claims 50-68 and 70-77 are amended to recite -- plasmid DNA-- polynucleotides. Applicants respectfully reserve the right to pursue additional subject matter supported within this specification in one or more future continuing applications.

Claims 50, 54 and 74 are further amended to address §112, second paragraph concerns as discussed *infra*.

Applicants are pleased to note that the full set of drawings entered on 03 March 2003 and replacement sheets for Figures 6E, 7E and 11D entered on 17 February 2004 have been deemed acceptable.

Applicants again respectfully reiterate that the continuing data for this application, as entered in the Amendment mailed 12 April 2002, should read as follows:

> This application is a continuation of U.S. application serial no. 08/702,502, which is the §371 U.S. national phase prosecution of PCT international application serial no. PCT/US95/02633, filed March 3, 1995, now abandoned, which is a continuation-in-part of U.S. application serial no. 207,526, filed March 7, 1994.

Rejection of Claims 50 and 51 Under 35 U.S.C. §102(e)

Claims 50 and 51 stand rejected under 35 U.S.C. §102(e) as allegedly "being anticipated by Goldsmith et al (U.S. Patent No. 5,861,290; see the entire reference)." Applicants disagree, respectfully taking the position that Goldsmith et al (U.S. Patent No. 5861,290; herein "the '290 patent") does not disclose, teach or suggest the presently claimed bi- or tri-cistronic polynucleotide vector construction for *in vivo* mammalian administration. The following discussion supports this notion.

First, the '290 patent discloses vectors and methodologies requiring three elements, with the actual vector (polynucleotide) in question comprising only two of these three elements. This vector comprises a cis-acting regulatory element (element 1) fused upstream of a *first (and only)* cistron (element 2), referred to in the '290 patent as the "effector gene." Expression of the effector gene relies on the interaction of a trans-acting regulatory factor (element 3) with the cis-acting sequence. The trans-acting factor (supplied from within the target cell) interacts with the cis-acting sequence to promote expression of the effector gene.

The '290 patent specifically teaches that the cis-acting element is chosen on the basis of the predicted presence of the trans-acting factor as a result of the cell being effected by a "hyperproliferative disorder or infection from an infectious agent". Therefore, the '290 patent teaches a therapeutic methodology which relies on a *standard* gene therapy/gene delivery system: that being a cis-acting promoter fused upstream of the coding region of the gene of interest, in this case referred to as an "effector gene." The only arguably novel portion of the '290 patent disclosure is the strategy of relying on the 'pre-expression' of a 'disease-associated' trans-acting factor within the host cell. Use of a cis-acting sequence known to interact with that specific trans-acting factor would then promote "effector gene" expression. Therefore, this system does not contemplate the delivery of more than one 'effector gene' to the target cell. Instead, as mentioned above, the '290 patent does nothing more than slightly advance the 'one gene, one promoter' system by adding the twist of matching up a disease associated regulatory factor with the appropriate cis-acting region to drive a sort of time-specific expression of a selected gene of interest.

Second, it should be noted that the invention as currently amended recites DNA plasmid based bi- and tri-cistronic polynucleotides which induce an immune response subsequent to *in vivo* mammalian administration. In contrast, the preferred vector system disclosed in the '290 patent is a viral based vector system such as a replication defective retroviral vector. It is within this context that it respectfully becomes clear in distinguishing the present invention from two specific phrases forwarded in the present Office Action:

> "the specification teaches that recombinant retroviral vectors may also be formulated for in vivo administration if they are replication defective and include HIV-derived vectors (e.g., an HIV-based retroviral vector expressing the env gene obtained from HIV-1_{SF162}) (e.g. column 15, lines 20-45; claims 13-19)."[1]
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> "[T]he replication defective HIV-derived vectors taught by Goldsmith et al necessarily comprise multiple cistrons present within the vector that express multiple proteins in animal cells in culture and which would reasonably be expected to express multiple gene products (e.g., gp160env and a selection marker) if introduced into at least some mammalian cell types in vivo".[2]

[1] 5/4/04 Office Action, last four line of last complete paragraph of page 3.
[2] 5/4/04 Office Action, bridging paragraph of page 3 through page 4, line 2.

The invention as presently claimed is not anticipated by the '290 patent. The "HIV-based retroviral vector expressing the env gene obtained from HIV-1_{SF162}" do not originate from a single vector. Instead, the 'retroviral vector' described within the bulk of the '290 patent comprises as one component a selectable marker gene. The HIVenv gene/protein (e.g., HIV-$1_{SF162)}$ is not supplied on this vector, but instead part of a series of vectors utilized in a retroviral packaging cell line (see Example 7; column 21, lines11-18). These separate expression vectors (including the "retroviral vector" containing an "effector gene") are then transfected into a cell line of choice. These 'helper plasmids' encode relevant portions of the retroviral genome required to effect subsequent infection of the target cell. Therefore, any HIV component of this system is (1) provided on a separate vector and (2) provided to address cell tropism issues and not to generate an immune response against the HIV envelope protein. Therefore, Applicants respectfully take the position that the '290 patent does not anticipate claims 50 and 51, either in the earlier form or in the form currently amended. To this end, Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 50-54 and 74 Under 35 U.S.C. §102(e)

Claims 50-54 and claim 74 stand rejected under 35 U.S.C. §102(e) as allegedly "being anticipated by Hu et al (U.S. Patent No. 6,107,062; see the entire patent)." Applicants respectively disagree and overcome the present rejection for essentially the same reasons as discussed in the previous section regarding the §102(e) rejection of claims 50 and 51 in view of the '290 patent. This rejection is overcome by amendment to claims 50-74, currently amended to recite a DNA plasmid-based construct for *in vivo* mammalian administration. Similar to the '290 patent disclosure Hu et al (herein, "the '062 patent) disclosure the use of a viral-based vector system to deliver and express antisense fragments for the purpose of effecting expression of disease genes. More specifically, the '062 patent disclosure purports the use of an HIV replication defective virus carrying an antisense sequence or encoding an antisense ribozyme for delivery to the target cell. The '062 patent does not anticipate, teach or suggest the DNA plasmid-based constructs of the present invention. Therefore, Applicants respectfully request withdrawal of this rejection.

Rejection of Claims 50-63 and 74 Under 35 U.S.C. §112, Second Paragraph

Claims 50-63 and 74 stand rejected under 35 U.S.C. §112, second paragraph as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants respectfully overcome the specific nature of these rejections by amending claims 50 and 74 to more precisely recite a DNA plasmid polynucleotide which contains either two or three cistrons; the first two required and the third optional. In addition, claim 54 is currently amended to include Markush language so as to provide recite a clear and concise grouping for the various HIV antigens contemplated in claim 54. In view of currently amended claims 50, 54 and 74, Applicants respectfully request reconsideration and withdrawal of this §112, second paragraph rejection.

In view of the comments *supra* and amendment to claims 50-68 and 70-77, Applicants respectfully take the position that all pending claims are in proper form for allowance. Early action to that end is earnestly solicited. The Examiner is invited to contact the undersigned attorney if clarification is required on any aspect of this response, or if any of the claims are considered to require further amendment to be placed in condition for allowance after entry of this Amendment.

Respectfully submitted,

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